# Breast-feeding after breast cancer: if you wish, madam

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REVIEW

# Breast-feeding after breast cancer: if you wish, madam

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**Abstract** Breast cancer is the most common malignant tumor-affecting women during the child bearing period. With the rising trend in delaying pregnancy later in life, the issue of subsequent pregnancy and lactation following breast cancer diagnosis has been more frequently encountered. In this context, data is scarce particularly those addressing the issue of lactation. In this review, we discussed different endocrinal, clinical and biological aspects dealing with breast-feeding after breast cancer in an attempt to determine how safe and feasible this approach is.

**Keywords** Breast cancer · Breast-feeding · Survival · Pregnancy · Safety · Young women · Prolactin

## Introduction

Breast cancer is the most common malignant tumor in females, affecting one in nine healthy women [1]. The median age of developing breast cancer varies from one part of the world to another; with 10% of patients in the developed world and 25% in the developing world diagnosed below the age of 40 [2, 3]. These young women have a poorer overall survival and a doubled risk of recurrence compared to older patients [4]. However, with the advances in early diagnosis and tailored adjuvant therapies, breast cancer mortality has been decreasing in all age cohorts leading to more young women surviving their cancer [5]. Additionally, there has been a trend toward delaying pregnancy until later in life [6] and thus the issue of subsequent pregnancy and breast-feeding is becoming more relevant and worth consideration.

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## Pregnancy after breast cancer

Pregnancy after breast cancer diagnosis is controversial, particularly regarding its safety. Formerly, it was assumed that the high estrogen levels during pregnancy might increase the risk of disease recurrence and thus pregnancy was not recommended. This belief was reinforced because young women carry poorer prognosis and from uncertainties about fetal health following maternal chemotherapy and/or radiotherapy. Since prospective randomized trials are not feasible, the available evidence comes from retrospective case series and case control studies. Quite unexpectedly, data from these trials suggest that subsequent pregnancy does not have a detrimental effect on survival or local relapse [7]. Even more, there is a suggestion that pregnancy might have a protective effect [8, 9]. Several theories have been posed to explain this finding including patient selection, the healthy mother effect [9], alloimmunization [10] and estrogen-induced apoptosis of the endocrine responsive breast cancer cells [11]. Pregnancy is now generally deemed safe 1–2 years following breast cancer diagnosis [7].

## Breast changes during pregnancy and lactation

The breast is one of few organs that undergoes most of its development during and after pregnancy. Estrogen, progesterone and prolactin are involved in this process and their influence is exerted via binding to target receptors on the breast. During early pregnancy, the levels of progesterone, prolactin and placental lactogen rise leading to the expansion of the terminal duct lobular units. During mid-pregnancy secretory differentiation begins with a rise in the mRNA of many milk proteins and enzymes responsible for milk production. This switch to secretory differentiation is called stage I lactogenesis [12]. Hormonal regulation of this state is not well understood, but candidate hormones are progesterone, prolactin, placental lactogen and possibly growth hormone. The gland remains quiescent governed by the high progesterone level supplied from the placenta. Progesterone acts as the main inhibitor of milk production and when this hormone decreases after birth, stage II lactogenesis begins, governed as well by high prolactin levels. As suckling starts, there is an additional increase in the expression of genes involved in milk secretion with further expansion of the alveolar epithelium [13] (Fig. 1). Following initiation, lactation is maintained by continuous removal of milk from the breast and is governed by two hormones; prolactin and oxytocin. The former acts on the luminal epithelial cells to sustain milk secretion, while the later acts on the myoepithelial cells to facilitate milk ejection. After weaning and termination of suckling stimulus, the terminal duct lobular unit involutes with apoptosis of a large proportion of the alveolar cells and remodelling of the gland, thus returning back to the mature pregnant quiescent state [14].

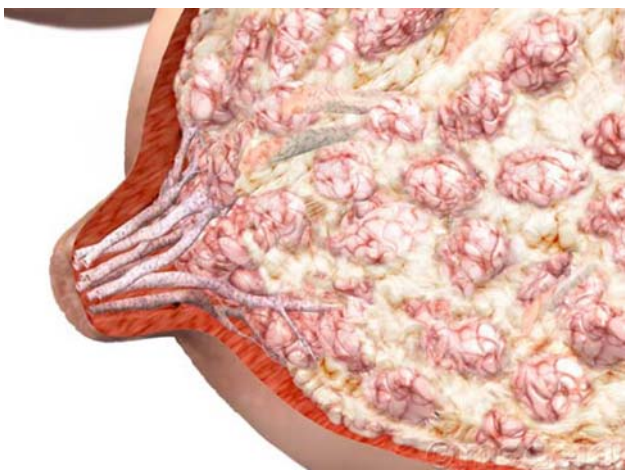

**Fig. 1** The lactating breast (Medela AG, Switzerland 2006)

## General aspects of breast-feeding

Currently, there is large and growing body of evidence suggesting that breast-feeding provides immediate and long lasting health advantages for both the infant and the mother. Breast-fed newborns have been found to suffer lower rates of neonatal infections, autoimmune diseases, allergies and subsequent risk of childhood obesity compared to bottle fed babies [15]. Data also suggest that the breast-fed newborns have better neuropsychological development [16]. In a meta-analysis of 20 studies, breast-fed babies had significantly higher scores for cognitive development compared to those receiving human milk substitutes [17]. Lactation provides an opportunity for the mother to naturally bond with her newborn. It also facilitates weight loss following pregnancy, helps the control of postpartum bleeding, stimulates the uterus to contract back to its original size, as well as adjusting blood glucose profiles in women with gestational diabetes [18]. In addition to all these advantages, breast milk is always clean, warm, ready to use and hence free! All these considerations have led numerous health and social organizations to promote and encourage the practice of breast-feeding.

## Lactation and breast cancer: epidemiological evidences

There has long been controversy regarding the effect of breast-feeding in reducing breast cancer incidence. A literature review by Lipworth et al. [19], concluded that women who nursed their children had a reduced incidence of breast cancer compared to those who did not, with a clear inverse relationship between duration of lactation and breast cancer incidence. In 2002, the Collaborative Group on Hormonal Factors and Breastfeeding conducted the largest analysis evaluating the effect of breast-feeding on breast cancer incidence in healthy women [20]. They analyzed 47 case–control and cohort studies from 30 different countries, which included at least 100 women with subsequent breast cancer. The relative risk reduction of breast cancer incidence was 4.3% (95% CI: 2.9–5.8; $P < 0.0001$) for each year of breast-feeding. Subgroup analyses found no difference related to age, menopausal status, ethnicity, parity, age at first delivery, body mass index. The authors speculated that breast cancer incidence in western countries could be halved (from 6.3 to 2.7% at 70 years of age) if parity and lactation habits were similar to those of developing countries.

Among women with BRCA1 mutation, the protective effect may be even stronger [21]. In 2004, Jernstrom et al. reported the results of a retrospective case control study of breast-feeding and subsequent breast cancer in 685 BRCA1 and 280 BRCA2 mutated women [22]. Although breast-

feeding duration was shorter in BRCA1 mutation carriers compared to non carriers (6.0 vs. 8.7 months, 95% CI: 1.4–4.0; $P < 0.001$), women with BRCA1 mutation who breast fed their babies for more than one year had a 45% reduction in the risk of developing breast cancer compared to women who never breast fed (OR 0.55 95% CI: 0.38–0.80, $P = 0.001$). However no protective effect was shown in BRCA2 mutation carriers.

## Breast-feeding associated with a reduction of breast cancer incidence: biological hypotheses

Several hypotheses have been postulated to explain the protective value of breast-feeding on breast cancer incidence.

### Excretion of carcinogens

Some data suggest that lactation can reduce the carcinogen level in the breast [23]. Human milk is quite rich in fat and lipophilic substances such as organochlorines diminish during lactation [24], thus possibly reducing the risk of developing breast cancer. Additional evidence of the local effect of breast-feeding is provided by the study by Ing et al. who reported a fourfold decrease of breast cancer incidence in the right breast, traditionally used in the Far East as the unique site of breast feeding [25].

### Anovulatory cycles

During breast-feeding, suckling interferes with the hypothalamus-pituitary axis. Pulsatile secretion of luteinizing hormone (LH) from the pituitary is inhibited as GnRH secretion is perturbed [26]. Thus, only small follicles develop in the ovaries with reduced estradiol levels and amenorrhea. Moreover, the hypothalamus-pituitary-gonadal axis is hypersensitive to the negative feedback effect of estradiol maintaining low gonadotrophins levels [27]. Lactational amenorrhea varies in duration according to suckling habits, and is one of the postulated protective mechanisms of breast-feeding with regards to breast cancer incidence. Other studies [28] have suggested that the risk of breast cancer is related to the cumulative number of menstrual cycles from first pregnancy to menopause. Breast-feeding longer than 3 months has been associated with a reduction in breast cancer incidence of 16% (95% CI: 0.71–0.99).

### Differentiation of mammary tissue

Animal model research suggests that terminal differentiation of the mammary gland, as observed during pregnancy and lactation, protects ductal cells from carcinogen-induced transformation [29]. In these experiments, breast carcinogenesis was initiated by chemicals which reacted with a highly proliferative and undifferentiated mammary epithelium [30].

### Prolactin

As previously mentioned, prolactin appears to be a key hormone involved in both mammary development and lactation. It is secreted by the anterior pituitary gland, although other non-pituitary tissues also synthesize prolactin, including the breast [31]. Extensive laboratory research has explored whether prolactin can influence the initiation and promotion of breast cancer. The results of this research has been inconclusive. Some reports suggest there is a mitogenic effect of prolactin on mammary tumour cells [32], but others propose that prolactin acts against angiogenesis [33], suppresses invasion and inhibits epithelial transition and cell proliferation [34]. The controversy is even more pronounced in epidemiological studies with some arguing that elevated serum prolactin in healthy women increases breast cancer risk [35, 36]. Such diversity of theories might discourage oncologists from promoting the practice of breast-feeding among their breast cancer patients.

Clinical evidence from the early seventies and eighties ironically might settle the debate. There was anecdotal evidence of breast cancer regression following pituitary stalk section [37]. One study found long term highly elevated prolactin following surgery with a disappearance of pulmonary metastases, suggesting that elevated prolactin did not stimulate progression and may even potentiate regression. In a later study, postoperative prolactin elevation was associated with improved survival for postmenopausal patients with node-negative disease [38]. Wang et al. concluded that women whose prolactin level fell postoperatively had significantly shorter overall survival compared with those who had a persistent elevation for 10 days ($P < 0.005$). Furthermore, in a recent study, activated Stat5, a key prolactin-induced transcription factor [39], was significantly associated with better prognosis breast cancer [40]. Thus prolactin may have a role in reducing breast cancer incidence [41].

In addition to the previously mentioned hypotheses, other points require cautious interpretation. Breast tissue remodelling after weaning has been correlated with a temporary increase in breast cancer incidence, possibly due to apoptotic changes of the lactating epithelium together with stromal activation. This hypothesis remains speculative, but warrants cautious follow up of patients for one year from pregnancy or lactation [42].

### Effect of breast-feeding in women with previously diagnosed breast cancer: clinical perspective

As mentioned earlier, several trials have addressed the effect of pregnancy on survival following breast cancer. However, only one study reported the proportion of patients who actually breast fed their children [43]. In this retrospective case control trial conducted by the International Breast Cancer Study Group (IBCSG), 94 women who gave birth following breast cancer diagnosis had an improved survival over their matched controls (risk ratio: 0.44; 95% CI: 0.21–0.96; $P = 0.04$). Data on breast-feeding were reported by the referring oncologist and lacked details about duration, exclusiveness, and site of lactation in cases of breast conserving surgery. Nonetheless, 27 of the 94 women were reported as having breast fed, 25 were reported as having bottle fed their babies, and 42 had unknown nursing status. Breast-feeding was not considered in the original survival analysis, but a recently requested review suggested that breast-feeding was not detrimental, but rather was associated with better survival (Fig. 2). Nevertheless, these data must be interpreted with caution due to many possible biases (physicians and not women reported breast-feeding habits, for example); however, the results are reassuring.

Apart from safety considerations, feasibility of nursing remains of concern. An important issue is how to manage breast feeding with unilateral milk production or reduced milk production from the irradiated breast. As more young women have breast conserving surgery and subsequent radiotherapy, the long-term effects of surgery and ionizing radiation on the mammary gland have become increasingly important. In an early report by Higgins and Haffty [44], only four out of ten patients were able to lactate from the treated breast, while no similar problems were encountered in the contralateral breast. Tralins [45] reported that 34% of patients had at least some milk production from the irradiated breast, but only 13/18 women chose to breastfeed. Of the five who did not breastfeed, three reported insufficient milk as a reason. Moran et al. [46] retrospectively analyzed over 3,000 patients from their hospital treated from 1965 to 2003 and were able to identify 29 pregnancies in 21 patients (one patient had bilateral breast cancer); four women elected pharmacological suppression of lactation. Out of the remaining 18 breasts, lactation occurred in 10 (55.6%), did not occur in seven (38.9%) and was unknown in one (5.5%). Breast volume was reported as significantly diminished in 80% of treated breasts. This observation is consistent with that of our group and is probably related to radiotherapy-induced fibrosis (Fig. 3)

The proximity of the incision to the areola and nipple, the location of the tumor, the dose and type of radiotherapy are all contributing factors to lactation success from the treated breast [47]. Patients and physicians should be informed that milk produced by one breast is sufficient for the nutritional need of the newborn. The experience of mothers who choose to use only one breast for exclusive breast-feeding, validates this notion [25], together with the historical habit of wet nursing of more than one child [48]. The mother should be reassured about the adequacy of milk production by a single breast and encouraged to seek early advice if latching problems occur.

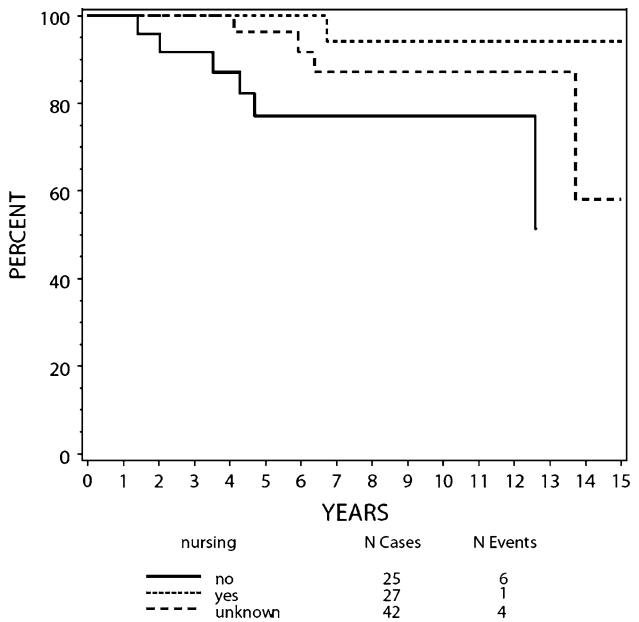


**Fig. 2** Overall survival by physician report of lactation (Gelber et al. [43] with permission)

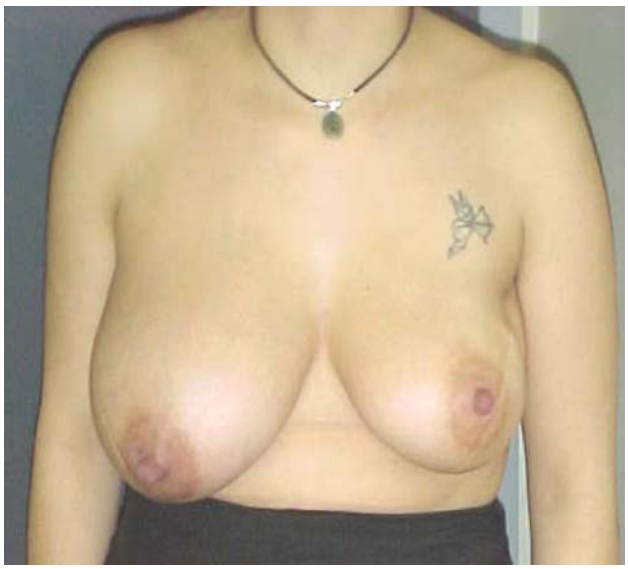

**Fig. 3** Breast asymmetry in a woman at 23 weeks gestation following left quadrantectomy and radiotherapy

## Special issues for breast-feeding mothers with previous breast cancer

Maternal counseling remains pivotal in successful breast-feeding. History of breast cancer makes counseling more demanding due to the concerns among the social and medical community about the safety of such approach. As each breast can control the rate of milk synthesis independently from the other [49], failure to nurse from one breast should not affect the use of the other. In our experience, most women who breast fed their babies after breast cancer used the healthy breast even if the irradiated breast had some milk production (data not shown). In these cases, maternal education on methods to help the infant open his/her mouth widely to grasp the areola (150° at the angle of the mouth) is essential [50]. Lactating mothers should be advised to offer the breast as many times as requested by their infants, and use the electric pump if the baby does not empty the breast completely [51]. Side-lying holds, focusing on the areola and nipple may also result in easier latching. Frequent changes in the positioning of the baby improve breast drainage in all quadrants, thus reducing the risk of engorgement and increase milk production. If pain or nipple abrasions occur, the mother should improve the baby's latch-on, trying to cover the entire nipple-areola complex with the baby's mouth and seek professional advice.

There is no evidence that long-term lactation interferes with breast examination or radiological evaluation. Ultrasound can be safely and effectively performed during lactation and mammogram or breast magnetic resonance can be done after having drained the lactating breasts [52].

Last but not least, breastfeeding provides a unique interaction between mother and child, providing a strong maternal empowerment, which can contribute to complete psychological rehabilitation for breast cancer survivors [53].

## Conclusions

Available endocrine and clinical evidence support women with history of breast cancer safely nursing their babies. Those who were subjected to mastectomy can breast-feed from the normal breast. Others who had conservative breast surgery can try to breast-feed also from the treated breast, although the likelihood of failure is around 40%. As stated in the SOGC clinical practice guidelines [54]: "There is no evidence that breast-feeding increases the risk of breast cancer recurring or of a second breast cancer developing, nor that it carries any health risk for the child. Women previously treated for breast cancer who do not show any evidence of residual tumor should be encouraged to breastfeed their children." As oncologists, we should prioritize global women's health and encourage this approach.

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